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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/637,302	08/11/2000	John Hood	TSRI 710.2	8590

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EXAMINER
SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
1652	//

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/637,302	HOOD ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *7-13,17-40 and 42-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,14-16 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The preliminary amendment filed June 14, 2001 amending the specification to amend the title and insert the reference to Government support has been entered.

Claims 1-67 are pending.

Election/Restriction

Applicant's election with traverse of Group I, Claims 1-6, 14-16 and 41 in Paper No. 10 filed December 2, 2002 is acknowledged. The traversal is on the ground(s) that "the grouped claims are classified in either class 424, subclass 94.5, or class 514, subclass 44 ... Accordingly, a single search will provide pertinent art for the claims in Groups I, II, V, VI, IX, X, XIII, XIV, XVII and XVIII" (Remarks, page 1). Applicants further argue that in such cases according to the MPEP 808.02 "no reasons exist for dividing among related inventions" (page 2, emphasis added). This is not found persuasive because the MPEP 808.02 concerns with related inventions whereas inventions I, II, IX and X are unrelated as drawn to structurally and functionally different polypeptides (Office action mailed October 2, 2002, page 5).

With regard to inventions I and V or VI, etc., the restriction requirement did not assert that the inventions of Groups I and V or VI were independent of one another but instead admitted that these groups are related as product and process of use. However, MPEP 806.05(h) clearly addresses the requirements for showing when

inventions which are related as product and process of use are patentably distinct and thus divisible. As previously stated inventions which are related as product and process of use inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the protein can be used as a kinase or to induce antibodies and the method can be practiced with the products of Groups III, IX and XI. Furthermore, while the inventions of the two groups may be classified in the same subclass, the search for the two groups is not identical. Search of the elected group would require search of information with regard to compositions of the Raf proteins for any pharmaceutical purposes while search of Group V or VI would require search for information directly linking the Raf proteins to angiogenesis.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-13, 17-40 and 42-67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Information Disclosure Statement

The instant application contains no IDS.

Specification

The amendment filed June 14, 2001 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: in the title "protein kinase Raf" was replaced with "tyrosine kinase Raf". Applicants did not indicate support for this amendment. Furthermore, Raf is a serine/threonine kinase not tyrosine kinase.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Objections

Claims 1-6 and 14-16 are objected to under 37 CFR 1.75(d)(1) as being in improper form because the claim states an improper Markush group. Compounds included within a Markush group must (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility (See MPEP ° 803.02.) The current claims recite "pharmaceutical composition [that] comprises a Raf protein or an oligonucleotide having a nucleotide sequence capable of expressing said protein". The members of the Markush group, a protein and an oligonucleotide meet

neither requirement, supra, because a protein and an oligonucleotide are structurally and functionally different and have different utilities (Office action mailed October 2, 2002, page 6).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 14-16 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in the recitation of "Raf protein" or "Raf". The specification defines the terms "Raf protein" or "Raf" as referring "collectively to the various forms of protein kinase Raf protein" (page 13, lines 11-13). The specification does not clearly define the metes and bounds of either "Raf" or "various forms". While the art clearly discusses a number of particular proteins of the Raf gene family, applicants clearly intend these terms to include a wide variety of mutants, derivatives and fragments of these proteins without any definition of the scope "Raf" and "various forms thereof" encompassed (e.g., Monia et al., US Patent 5,952,229, column 1, lines 21-34). It is not defined which necessary structural and/or functional features a protein must possess to be a "Raf protein". It is assumed that these terms imply some level of

structural homology to human c-Raf protein having the amino acid sequence of SEQ ID NO:2 of the instant invention. However, it is unclear what are other sequences besides SEQ ID NO:2 that are included in the scope rendering the metes and bounds of the claims indefinite.

Similarly, Raf-caax or Raf-Caax (as on page 49, lines 24-25) are indefinite because it is not defined which sequences in addition to SEQ ID NO:7 are encompassed.

Claim 4 is confusing as drawn to a Raf fusion protein while it depends on claim 3 which is drawn to wild-type Raf. Wild-type Raf is not a fusion protein.

Claims 14-16 recite the limitation " said administering". There is insufficient antecedent basis for this limitation in the claims because claim 1 from which claims 14-16 depend does not recite "administering".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 41 is rejected under 35 U.S.C. 102(a) as being anticipated by Skopinska-Rozewska et al.

Skopinska-Rozewska et al. teach angiogenesis induced in mice by urothelial cells (HCV-29) transfected with polynucleotide encoding v-raf. V-raf transfected HCV-29 cells produce v-raf having kinase activity and represent a pharmaceutical composition comprising thereof.

Claim 41 is rejected under 35 U.S.C. 102(b) as being anticipated by Zhou et al.

Zhou et al. teach angiogenesis induced by a membrane-targeted raf kinase (raf-CAAX) in human breast carcinoma cells. Raf-caax added to the cells represents a pharmaceutical composition comprising thereof.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 14-16 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou et al.

The teachings of Zhou et al. are outlined above. Because Zhou et al. teach the induction of angiogenesis by a Raf fusion protein, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce an article of manufacture such as a kit for modulating (potentiating) angiogenesis, said article comprising Raf protein.

Since the effect of Raf-Caax is caused by Raf, it would have been obvious to one of ordinary skill in the art to substitute a fusion protein with a wild-type Raf depending on the availability (claim 3).

It would have been obvious to one of ordinary skill in the art to administer a pharmaceutical composition by any route known and used in the art. For some routes of administration it would have been obvious to produce the composition in the form of a liposome.

One of ordinary skill in the art would have been motivated to use such article of manufacture for potentiating angiogenesis in treating conditions such as poor circulation that would benefit from neovascularization.

Claims 1-4, 6, 14-16 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monia et al.

Monia et al. (US Patent 5,952,229, *supra*) teach the importance of Raf proteins in abnormal proliferative conditions including angiogenesis (column 3, lines 19-62). They teach the DNA sequence encoding human c-Raf protein (SEQ ID NO:64) that is 100% identical to SEQ ID NO:1 of the instant invention that encodes SEQ ID NO:2.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce an article of manufacture such as a kit for modulating (potentiating) angiogenesis, said article comprising Raf protein such as encoded by SEQ ID NO:64.

It would have been obvious to one of ordinary skill in the art to use Raf protein in a form of a fusion protein with a reporter or target binding molecule, for example.

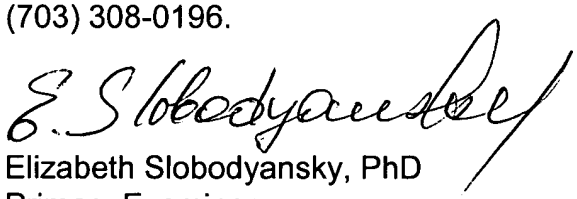
It would have been obvious to one of ordinary skill in the art to administer a pharmaceutical composition by any route known and used in the art. For some routes of administration it would have been obvious to produce the composition in the form of a liposome.

One of ordinary skill in the art would have been motivated to use such article of manufacture for potentiating angiogenesis in treating conditions such as poor circulation that would benefit from neovascularization.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.



Elizabeth Slobodyansky, PhD
Primary Examiner

February 20, 2003